Citation:

Trevisan M, Cooper R, Ostrow D, Miller W, Sparks S, Leonas Y, Allen A, Steinhauer M, Stamler J. Dietary sodium, erythrocyte sodium concentration, sodium-stimulated lithium efflux and blood pressure.*Clin Sci (Lond)*. 1981 Dec; 61 Suppl 7: 29s-32s.

PubMed ID: 7318331

Study Design:

Study 1: Cross-sectional; Study 2: Randomized trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEGATIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To explore the relationships between dietary sodium, erythrocyte sodium metabolism and blood pressure (BP) in pre-adolescent and adolescent youngsters.

Inclusion Criteria:

- Study 1, observational study: African American school children between age 11 and 15 years in the parochial schools of Chicago that had participated in a previous BP survey
- Study 2, experimental study:
  - Students from a Seventh Day Adventist boarding high school
  - Consuming a lacto-ovo-vegetarian diet.

Exclusion Criteria:

- Study 1, observational study:
  - Not an African American child
  - Not between age 11 and 15 years
  - Had not participated in a previous BP survey in the parochial schools of Chicago
- Study 2, experimental study:
  - Not a student from a Seventh Day Adventist boarding high school
  - Not consuming a lacto-ovo-vegetarian diet.

Description of Study Protocol:

Recruitment

- Study 1: 29 African American students from parochial schools in Chicago that had

participated in a previous BP survey
- Study 2: 21 students from a Seventh Day Adventist boarding school who were consuming a lacto-ovo-vegetarian diet.

Design

- Study 1:
  - Seven consecutive 24-hour urine collections were obtained from study subjects
  - Blood pressures were measured on two occasions during the week of urine collections
  - Weight was measured without shoes
  - Blood samples were collected and sodium-stimulated lithium efflux was determined using the method of Canessa, et al
  - Erythrocyte sodium concentration was measured
- Study 2:
  - 21 students students were randomly assigned to control or experimental group
  - The control group (N= 9) continued to eat standard school cafeteria meals
  - Study group (N=12) ate meals consisting of approximately 70% sodium of the standard meals
  - During the study, random 24-hour urines were collected and random duplicate meals were analyzed for sodium content
  - Erythrocyte sodium concentration was determined.

Dietary Intake/Dietary Assessment Methodology

Meals were randomly assessed for sodium content (method not described).

Intervention

- Study 1: No intervention
- Study 2: Study group was given a diet with 30% less sodium than control group,

Statistical Analysis

Paired T-testing within each group and T-testing across the two groups.

Data Collection Summary:

Timing of Measurements

- Study 1:
  - 24-hour urine samples were collected for seven days
  - BP was taken twice during the seven days
  - Timing of blood sample was not described, but assumed to be on day seven
- Study 2:
  - Baseline data collected day one (weight, BP)
  - Groups were randomized to study or control
  - Moderate salt restriction for 24 days (decrease from 216mmol to 72mmol sodium a day)
  - BP measured on first and last day
  - Random 24-hour urine samples collected
  - Random meals analyzed for sodium
  - Blood collection timing not specifically given but assumed as last day of study.

Dependent Variables

- Study 1:
  - Variable 1: Erythrocyte sodium concentration (determined after washing packed cells three times with iso-osmotic cold solution of MgCL2)
  - Variable 2: Systolic blood pressure (on each occasion, measured twice, one minute apart, a random zero sphygmomanometer used after a five-minute rest, cuff size based on arm circumference)
  - Variable 3: Urinary sodium excretion (measured by flame photometry)
  - Variable 4: Weight (measured in light street clothing without shoes)
  - Variable 5: Sodium stimulated lithium efflux (determined by method of Canessa, et al
- Study 2:
  - Variable 1: Erythrocyte sodium concentration
  - Variable 2: Systolic blood pressure (SBP)
  - Variable 3: Weight.

Independent Variables

- Study 1: No independent variables (observational study)
- Study 2: Low-sodium diet.

Description of Actual Data Sample:

- Initial N:
  - Study 1: N=29, 10 males, 19 females
  - Study 2: N=21 (sex not designated)
- Attrition (final N): No attrition reported for either study
- Age:
  - Study 1: Age 11 to 15 years
  - Study 2: Age not designated (identified as high school students)
- Ethnicity:
  - Study 1: African American
  - Study 2: Ethnicity not designated
- Other relevant demographics:
  - Study 1: Sample taken from parochial school in Chicago
  - Study 2: Sample taken from students of a Seventh Day Adventist boarding school, providing a lacto-ovo-vegetarian diet
- Anthropometrics:
  - Study 1: Mean weight was 53.5±14.0kg
  - Study 2: No anthropometric data reported at baseline of conclusion of study
- Location: Private schools in Chicago.

Summary of Results:

Dietary Sodium, Erythrocyte Sodium Concentration, Sodium-stimulated Efflux from Cells and Blood Pressure

Observational Study N=29	Correlation Coefficeint	
	Na-simulated Li Efflux	Erythrocyte Sodium Concentration

SBP	0.512**	-0.107
Urinary Na (mmol per 24 hours)	0.060	-0.321*
Erythrocyte sodium concentration (mmol per L of cells)	-0.056	

Intervention Study	**Experimental N=12**	**Control N=9**
	Baseline Final	**Baseline Final**
Erythrocyte sodium concentration(mmol per L of cells)	8.01±1.1 7.41±1.0***	8.70±1.9 8.60±2.1
SBP (mmHg)	108.42±11.6 107.17±13.1	110.67±10.5 110.67±7.6

*P<0.05; **P <0.01; ***difference between baseline and final: P<0.01.

Other Key Findings

Study 1:

In 29 children:

- Mean weight was 53.5±14.0kg
- SBP: 105.5± 9.8mmHg
- Erythrocyte sodium concentration 8.9±2.0mmol per L of erythrocytes
- Sodium-stimulated lithium efflux (Li efflux) 3.2±0.9umol min-1 l-1 of erythrocytes
- Li efflux was positively and significantly correlated with SBP and the correlation remained significant with control for weight (R=0.487, P=0.05)
- Li efflux was not significantly (NS) related to erythrocyte sodium concentration or urinary sodium excretion
- Urinary sodium excretion was negatively and significantly correlated with erythrocyte sodium concentration
- Weight was significantly and directly correlated with BP.

Study 2:

- There was a significant decrease in erythrocyte sodium concentration in the experimental group at the end of the study period and virtually no difference was detectable in the control group
- The difference between the differences for the two groups was statistically significant
- Changes in SBP and weight did not reach statistical significance.

Author Conclusion:

Data presented support the hypothesis that a relationship exists between intracellular sodium metabolism and BP, and that some aspects of intracellular sodium metabolism are influenced by dietary intake.

Reviewer Comments:

- *This paper included reports on two completely different studies; one an observational study and one a RCT. It was unclear whether subjects in the two studies were related demographically or ethnically. Sample sizes were small and one group was African American while the second study involved lacto-ovo-vegetarian students from a Seventh Day Adventist School. Findings, if significant, could not be generalized to all adolescents*
- *The checklist was rated on a combination of the two studies with those questions that pertained to cross-sectional studies answered for Study 1 and those for RCT answered for Study 2*
- *This is a weak paper in that important baseline data on subjects were not reported. The discussion concentrated on others findings and very little discussion on the limitation of the authors' studies, which were many*
- *Another key limitation in study 2 is the short duration of study period (24 days).*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No

2.2.	Were criteria applied equally to all study groups?	???
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	???
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	No
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	???
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	???
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	Yes
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	No
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???

5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	???
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	???
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes

8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	???
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
8.6.	Was clinical significance as well as statistical significance reported?	No
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	???
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes